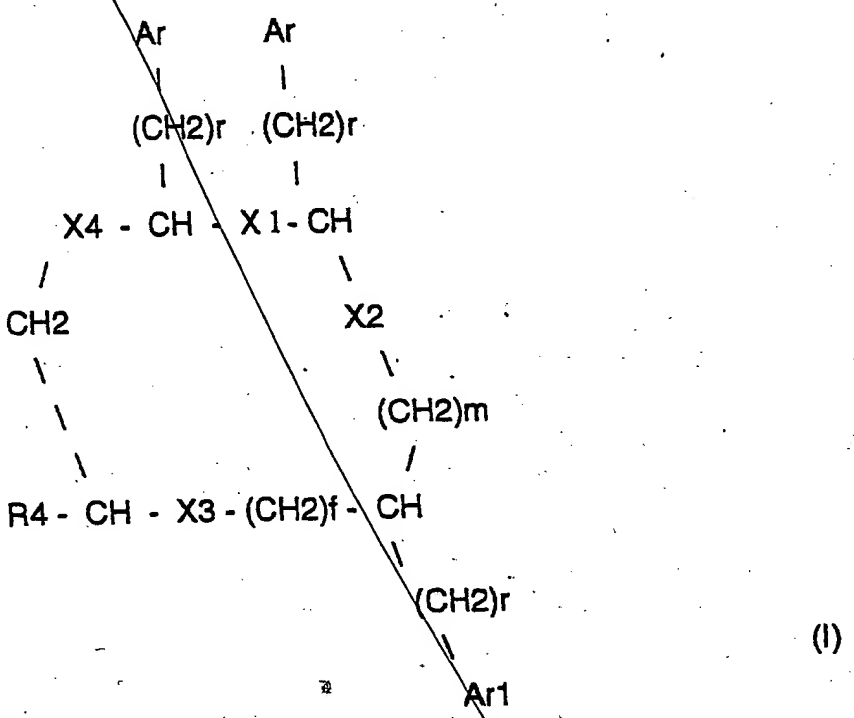
In the Claims

Please cancel claims 1-20, without prejudice or disclaimer.

Please add new claims 21-33, as follows:

--21. Monocyclic compounds of general formula (I)



(I)

wherein:

X_1, X_2, X_3, X_4 are the same or different, and are selected from the group consisting of -CONR-, -NRCO-, $-CH_2-NR-$, and $-NR-CH_2-$ where R is selected from the group consisting of H, C_{1-3} alkyl, and benzyl;

f, m, are the same or different, and is a number selected from the group consisting of 0, 1 and 2;

R_1 and R_2, are the same or different, and represent:

$-(CH_2)_r Ar$ where r is 0, 1 or 2 and Ar is an aromatic group selected from the group consisting of benzene, naphthalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan,

benzofuran, thiazole, benzothiazole, imidazole, benzoimidazole, optionally substituted with up to 2 substituents selected from the group consisting of C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} alkyloxy, C_{2-4} amino-alkyloxy, halogens, OH, NH_2, CN, and NR_6R_7, where R_6 and R_7, same or different, are H or C_{1-3} alkyl,

R_3 is $(CH_2)_rAr_1$ where r is 0, 1 or 2 and Ar_1 is an aromatic group selected from the group consisting of benzene, naphthalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, and benzimidazole,

optionally substituted with up to 2 groups selected from the groups consisting of C_{1-3} alkyl and haloalkyl, C_{1-3} alkyloxy and amino-alkyloxy, halogens, OH, NH_2, CN and NR_6R_7, where R_6 and R_7, same or different, are H or C_{1-3} alkyl,

R_4 is NR_8R_9, where R_8 is H or C_{1-3} alkyl; and

R_9 is selected from the group consisting of methanesulfonyl, tosyl, and tetrahydropyranyl, tetrahydrothiopyranyl optionally mono or di-substituted by oxygen on the S atom, piperidyl, optionally substituted on the N-atom by a C_{1-3} alkyl, C_{1-3} acyl, aminosulfonyl, or methanesulfonyl; or a group $(CH_2)gR_{10}$ where g is 1,2, or 3 and R_{10} is selected from the group consisting of morpholine, furan and CN;

or R_8 and R_9 together with the N atom to which they are linked form a piperazine substituted on one of its nitrogens by a C_{1-3} alkyl, C_{1-3} acyl or methanesulfonyl;

$-N(R_{11})CO(CH_2)_hR_{12}$ where R_{11} is H or C_{1-3} alkyl; h is 0, 1, 2 or 3; and R_{12} is selected from the group consisting of morpholine, pyrrolidine optionally substituted with a hydroxy or hydroxymethyl, piperidine optionally substituted with a 4-hydroxy, 4-carboxyamido or 4-aminosulfonyl group, piperazine optionally substituted on the N-atom by C_{1-3} alkyl, triazole, tetrazole, 5-mercapto-tetrazole, furan, thiophene, thiomorpholine, optionally mono or di-oxygenated on the S-atom, and amino- cyclohexane optionally substituted on a hydroxy group;

- COR_{13} wherein R_{13} is a member selected from the group consisting of morpholine and piperazine optionally substituted by a C_{2-6} alkyl containing one or more ether or hydroxy groups;

their enantiomers and mixtures thereof, their diastereoisomers, and their pharmaceutically acceptable salts.

22. Compound according to Claim 21 wherein:

f is 1

m is 0

X_1, X_2, X_3, X_4, are the same or different and are a member selected from the group consisting of -CONR- and -NRCO-,

where R is H or methyl,

R_1 and R_2 are the same or different, are:

$-CH_2Ar$ wherein Ar is an aromatic group selected from the group consisting of benzene, pyridine, indole, optionally substituted with up to two residues with substituents selected from the group consisting of C_{1-3} alkyl and haloalkyl, C_{1-3} alkyloxy, C_{2-4} amino alkyloxy, halogens, OH, NH_2, CN, and NR_6R_7, where R_6 and R_7, same or different, and are H or C_{1-3} alkyl;

R_3 is $-CH_2Ar_1$ wherein Ar_1 is an aromatic group selected from the group consisting of alpha naphthyl, beta naphthyl, phenyl, phenyl substituted with up to two residues selected from the group consisting of C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3}alkyloxy, halogens, OH, and NH_2.

23. Compounds according to Claim 22 wherein:

- X_1, X_2, X_3, X_4 are -CONH-,
- R_1 is indol-3-yl-methyl
- R_2 is phenyl-methyl optionally substituted with up to two residues selected from the group consisting of chlorine, fluorine, CF_3, OH, CN, 3-pyridyl-methyl and 4-pyridyl-methyl;
- R_3 is benzyl.

24. Compounds according to claim 23 wherein:

R_4 is a group NR_8R_9 wherein:

R_8 is H or methyl;

R_9 selected from the group consisting of 4-tetrahydropyranyl, 4-tetrahydrothiopyranyl, 1-oxo-tetrahydrothiopyran-4-yl, 1,1-dioxo-tetrahydrothiopyran-4-yl, N-methyl-4-piperidinyl, N-methanesulfonyl-4-piperidinyl, and N-aminosulfonyl-4-piperidinyl,

or R_8 and R_9 together with the N atom to which they are linked represent N-methyl-piperazinyl, N-acetyl-piperazinyl or N-methanesulfonyl-piperazinyl.

25. Compounds according to Claim 24 represented by:

i) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

ii) cyclo{Suc[1-(S)-(4-tetrahydropyranyl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

iii) cyclo{Suc[1-(R)-(1-methyl-piperidin-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

iv) cyclo{Suc[1-(R)-(4-tetrahydrothiopyranyl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

v) cyclo{Suc[1-(R)-(1-oxo-tetrahydrothiopyran-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

vi) cyclo{Suc[1-(R)-(1,1-dioxo-tetrahydrothiopyran-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

vii) cyclo{Suc[1-(R)-N-methyl-N-(4-tetrahydropyranyl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

viii) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Tyr-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

ix) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe(4-F)-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

x) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe(3,5-F)-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xi) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe(4-CN)-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xii) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe(4-CF3)-[(R)-NH-CH (CH_2-C_6H_5)-CH_2NH]}

xiii) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Ala(4-pyridyl)-[R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xiv) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Ala(3-pyridyl)-[R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xv)cyclo{Suc[1-(R)-(1-methylsulfonyl-piperidin-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xvi)cyclo{Suc[1-(R)-(1-aminosulfonyl-piperidin-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xvii) cyclo{Suc[1-(R)-4-methyl-piperazin-1-yl]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xviii) cyclo{Suc[1-(R)-4-acetyl-piperazin-1-yl]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]} or

xix) cyclo{Suc[1-(R)-4-methylsulfonyl-piperazin-1-yl]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}.

26. Compounds according to Claim 23 wherein :

R_4 represents a group NR_8R_9, where R_8 is H and R_9 is methanesulfonyl, tosyl or a group $(CH_2)gR_{10}$, wherein g is 1 or 2 and R_{10} is morpholine, furan, or CN.

27. Compounds according to claim 26 represented by:

xx) cyclo{Suc[1-(S)-4-methylsulfonylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxi) cyclo{Suc[1-(R)-4-methylsulfonylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxii) cyclo{Suc[1-(S)-(4-methylphenyl)sulfonylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxiii) cyclo{Suc[1-(R)-(4-methylphenyl)sulfonylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxiv)cyclo{Suc[1-(S)-2-(4-morpholino)ethylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxv)cyclo{Suc[1-(R)-2-(4-morpholino)ethylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxvi) cyclo{Suc[1-(R)-(2-furyl)methylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]} or

xxvii) cyclo{Suc[1-(R)-cianomethylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}.

28. Compounds according to claim 23 wherein:

R_4 is a group - $N(R_{11})CO(CH_2)_h$-R_{12} wherein R_{11} is H, h is 0 or 1, and R_{12} is selected from the group consisting of 1-tetrazolyl, 5-mercapto-tetrazol-1-yl, 1-triazolyl, furanyl, thiophenyl, morpholine, 4-hydroxy-piperidine, 4-carboxyamido-piperidine, 3-hydroxy-pyrrolidine, 2-hydroxymethylpyrrolidine, 4-methyl-piperazine, 4-aminosulfonyl-piperazine, 1-oxo-

thiomorpholine, and 4-hydroxy-cyclohexan-1-yl-amino.

29. Compounds according to Claim 28 represented by:

xxviii) cyclo{Suc[1-(R)-2-(4-morpholino)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxix) cyclo{Suc[1-(S)-2-(4-morpholino)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxx) cyclo{Suc[1-(S)-2-(tetrazol-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxi)cyclo{Suc[1-(R)-2-(tetrazol-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxii) cyclo{Suc[1-(S)-2-(5-mercapto-tetrazol-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxiii) cyclo{Suc[1-(R)-2-([1,2,4]triazol-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxiv) cyclo{Suc[1-(R)-2-(furanyl)carbonylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxv) cyclo{Suc[1-(R)-2-(thiophen-3-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxvi) cyclo{Suc[1-(R)-(4-morpholino)carbonylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxvii) cyclo{Suc[1-(R)-2-(4-hydroxy-piperidin-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxviii) cyclo{Suc[1-(R)-2-(4-aminocarbonyl-piperidin-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xxxix) cyclo{Suc[1-(R)-2-(3-hydroxy-pyrrolidin-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xl) cyclo{Suc[1-(R)-2-(2-(S)-hydroxymethyl-pyrrolidin-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xli) cyclo{Suc[1-(R)-2-(4-methyl-piperazin-1-yl)acetylamino]-Trp-Phe-[(R)-NH-CH(CH_2-C_6H_5)-CH_2NH]}

xlii) cyclo{Suc[1-(R)-2-(4-methyl-piperazin-1-yl)carbonylamino]-Trp-Phe-[(R)-NH-CH(CH_2-

C_6H_5)-CH_2NH]}

xliii) cyclo{Suc[1-(R)-2-(4-aminosulfonyl-piperazin-1-yl)acetylamino]-Trp-Phe-[(R)-NH-$CH(CH_2$-$C_6H_5)$-CH_2NH]}

xliv) cyclo{Suc[1-(R)-2-(1-oxo-thiomorpholin-4-yl)acetylamino]-Trp-Phe-[(R)-NH-$CH(CH_2$-$C_6H_5)$-CH_2NH]} or

xlv) cyclo{Suc[1-(R)-2-*(trans*--4-hydroxy-cyclohexan-1-yl-amino)acetylamino]-Trp-Phe-[(R)-NH-$CH(CH_2$-$C_6H_5)$-CH_2NH]}.

30. Compounds according to Claim 23 wherein:

R_4 represents a group COR_{13} wherein R_{13} is a member selected from the group consisting of morpholine and 4-(hydroxyethyloxyethyl)-piperazine.

31. Compounds according to claim 30 represented by:

xlvi) cyclo{Suc[1-(4-morpholino)carbonyl]-Trp-Phe-[(R)-NH-$CH(CH_2$-$C_6H_5)$-CH_2NH]} or

xlvii) cyclo{Suc[1-(4-hydroxyethyloxyethyl-piperazin-1-yl)carbonyl]-Trp-Phe-[(R)-NH-$CH(CH_2$-$C_6H_5)$-CH_2NH]}.

32. Pharmaceutical compositions containing as active principle compounds of general formula (I) according to Claim 21 in combination with pharmaceutically acceptable carriers or excipients.

33. A method for the treatment of the bronchospastic component of asthma, cough, pulmonary irritation, intestinal spasms or local spasms of bladder, ureters during cystitis, kidney infections and colics wherein amounts of 0.1 to 10mg/kg body weight of an active principle represented by compounds of formula (I) according to Claim 21 are administered to the patient.

REMARKS

Reconsideration is respectfully requested in view of the foregoing amendments and the remarks which follow. Applicants have endeavored to address each of the issues raised by the Examiner and, by so doing, to advance the prosecution of the application to allowance.

Applicants have cancelled claims 2-15, 19 and 20 without prejudice or disclaimer, and have added new claims 21-33 inclusive all of which are fully supported in the as-filed